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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,891	03/31/2004	Maurice Arthur Trewella	GRH0105PUSA	7582
22045	7590	12/11/2007	EXAMINER	
BROOKS KUSHMAN P.C. 1000 TOWN CENTER TWENTY-SECOND FLOOR SOUTHFIELD, MI 48075			HA, JULIE	
		ART UNIT	PAPER NUMBER	
		1654		
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	10/814,891	TREWHELLA ET AL.
	Examiner	Art Unit
	Julie Ha	1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 27 October 2007.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-34 is/are pending in the application.
  - 4a) Of the above claim(s) 16-22, 24-30 and 34 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-15, 23 and 31-33 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.
 

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) Notice of Informal Patent Application
- 6) Other: \_\_\_\_\_

**DETAILED ACTION**

Amendment after Non-final rejection filed on October 27, 2007 is acknowledged. Claims 1-34 are pending in this application. Applicant elected without traverse Group I (claims 1-33) and species election of ketone, fluoxetine, ibuprofen and propylamine in the reply filed on March 22, 2007. Claims 16-22, 24-30 and 34 remain withdrawn from further consideration as being drawn to nonelected species (claims 16-22 and 24-30) and nonelected invention (claim 34). Claims 1-15, 23, and 31-33 are examined on the merits in this office action.

***Withdrawn Rejections***

1. Rejection of claim 1 and 12 under 35 U.S.C. 112, 2<sup>nd</sup> paragraph is hereby withdrawn due to Applicant's amendment. However, due to Applicant's amendment, new rejection under 35 U.S.C. 112, 2<sup>nd</sup> paragraph follows below.
2. Rejection of claims 1-2, 10-13 and 14-15 under 35 U.S.C 102(b) anticipated by Howarth et al is hereby withdrawn due to Applicant's amendment to the claims and persuasive arguments.
3. Rejection of claims 1 and 3-15 under 35 U.S.C. 103 unpatentable over Liu et al is hereby withdrawn due to Applicant's amendments to the claims and persuasive arguments.

After further consideration, anticipation rejection with Kumar et al reference has been revised to include claims 2-13 that was omitted in the previous office action.

***Maintained Rejection***

**35 U.S.C. 102**

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-15, 23 and 31-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Kumar et al (Tetrahedron Letters, 1991, 32(16): 1901-1904).

7. The instant claims are drawn to a method of reducing an organic compound (ketone), comprising subjecting the organic compound to a yeast mediated reduction wherein the reduction is conducted in the presence of water and in absence of any additional solvents. Further, the claims are drawn to the method wherein the compound is precursor for the synthesis of a pharmaceutical Fluoxetine.

8. Kumar et al teach a new chemoenzymatic synthesis of optically pure (R)-Tomoxetine and both the enantiomers of Fluoxetine (see abstract). The reference teaches baker's yeast reduction of ethyl 3-oxo-3-phenylpropanoate (ketone body) to yield ethyl 3-hydroxy-3-phenylpropionate (alcohol), the step comprising Baker's yeast, glucose, and water (see p. 1901, 3<sup>rd</sup> paragraph and p. 1902, Scheme, step (i)). This reads on claims 1 and 14-15. Since the reference teaches the reduction of starting material (ketone) into the final product (alcohol), the reaction must inherently have all of

water-to yeast ratio, temperature conditions, pressure, and must be under the same conditions (i.e., all of reaction conditions including separation steps). Therefore, this reads on claims 2-13. Further, the reference teaches the synthesis of Fluoxetine (aryl propylamine) (see p. 1902, Scheme, 2a and 2b). This reads on claim 23. Furthermore, it is well known in the art that Fluoxetine (Prozac<sup>TM</sup>, Eli Lilly Co.) is a potent clinically effective anti-depressant (see p. 1901, 1<sup>st</sup> paragraph, 2<sup>nd</sup> sentence). Thus, this reads on claims 31-33.

***Response to Applicant's Arguments***

9. Applicant argues that Kumar et al is deficient reference because "this reference fails to state the amount and nature of the contacting water." Applicant argues that "the Kumar et al. fails to disclose an amount of water that is sufficient for enzymes to be hydrated and but insufficient to provide a visible separate water layer." Furthermore, Applicant argues that "the presence of glucose in the compositions mitigates against the water being in a sufficient amount to only hydrate the enzymes as required by the present invention...glucose must likely be dissolved in the method of Kumar et al in order to be chemically useful."

10. Applicant's arguments have been fully considered but have not been found to be persuasive because Kumar reference teaches all of the components of the instant application. As described above, Kumar et al teach the reduction of ketone to an alcohol, as claimed. Since the starting material and the final product are made, it is inherent that the reference's method reaction was under the same reaction conditions

as claimed. In regards to the argument that "glucose must likely be dissolved in the method of Kumar in order to be chemically useful", since minimal amount of water is being used, it is inherent that glucose was dissolved in the water first before adding to the yeast. The specification of instant application describes reacting 10 g of yeast with 10 ml of water (see paragraphs [0075] and [0081]), 5 g of yeast with 5 ml of water (see paragraph [0079] and [0085]). The amount of water would be sufficient to dissolve the glucose in the reaction. The reference further teaches the final products (R)-Fluoxetine and (S)-Fluoxetine claimed by the instant application. Therefore, the reaction conditions used in the Kumar reference must be the same as the instant application, since water and yeast were used to reduce ketone to alcohol in step (i) to produce the alcohol precursor used to synthesize the final products. Therefore, the rejection is maintained.

***New Rejection***

***35 U.S.C. 112, 2<sup>nd</sup>***

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
12. Claims 1-2, 10-11, 13-15 and 31-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
13. Claim 1 recites, "a method of reducing an organic compound, the method comprising...in the presence of an amount of water that is sufficient for enzymes to be hydrated but insufficient to provide a visible separate water layer..." The phrase

"amount of water that is sufficient for enzymes to be hydrated but insufficient to provide a visible separate water layer" is unclear. It is unclear how much water would be enough to hydrate an enzyme. For example, it is unclear how one of ordinary skill in the art would know or determine how much water is sufficient to hydrate an enzyme but insufficient to provide a visible separate water layer. Claims 10-11 and 13-15 are dependent on claim 1, therefore, are included in the rejection.

14. Claim 2 recites, "...wherein the reduction is conducted in the presence of sufficient water to enable yeast mediated reduction to take place, but insufficient to provide a separate water layer." The phrase "in presence of sufficient water to enable yeast mediated reduction to take place" is unclear. It is unclear how much water would be enough to for the yeast mediated reduction to take place. For example, it is unclear how one of ordinary skill in the art would know or determine how much water is sufficient for yeast mediated reduction to take place, but insufficient to provide a visible separate water layer.

15. Claim 31 recites, "A method of synthesizing a pharmaceutical compound comprising... reduction is conducted in the absence of a solvent..." The phrase "absence of solvent" means. For example, it is unclear if "absence of solvent" means absence of organic solvent only or if means ALL solvents, including water. Claims 32-33 are dependent on claim 32, therefore, are included in the rejection.

### ***Conclusion***

16. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Ha whose telephone number is 571-272-5982. The examiner can normally be reached on Mon-Fri, 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

  
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PRIMARY EXAMINER